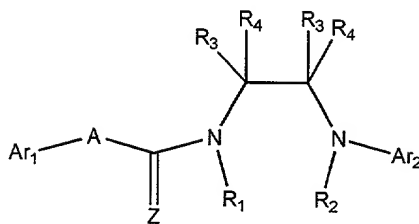


## Claims

**What is claimed is:**

1. A compound of the formula:



or a pharmaceutically acceptable salt thereof,  
wherein:

A is absent or is selected from the group consisting of O, S, NR<sub>A</sub>, CR<sub>B</sub>R<sub>B</sub>', NR<sub>A</sub>CR<sub>B</sub>R<sub>B</sub>', CR<sub>B</sub>R<sub>B</sub>'NR<sub>A</sub>, -CR<sub>A</sub>=CR<sub>B</sub>-, and C<sub>3</sub>H<sub>4</sub>; where R<sub>A</sub>, R<sub>B</sub>, and R<sub>B</sub>' are independently selected at each occurrence from hydrogen or alkyl;

Z is oxygen or sulfur;

R<sub>1</sub> and R<sub>2</sub> independently represent hydrogen or alkyl;

R<sub>3</sub> and R<sub>4</sub> are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted -S(O)<sub>n</sub>NHalkyl; optionally substituted -S(O)<sub>n</sub>N(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl;

optionally substituted  $\text{-NC(=O)(alkyl)(alkyl)}$ ; optionally substituted  $\text{-NHS(O)}_n\text{alkyl}$ ; optionally substituted  $\text{-NS(O)}_n\text{(alkyl)(alkyl)}$ ; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; or optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

$R_3$  and  $R_4$  not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S; and

$\text{Ar}_1$  and  $\text{Ar}_2$  are the same or different and independently represent optionally substituted cycloalkyl; an optionally substituted heterocycloalkyl ring of from 5 to 8 atoms, which heterocycloalkyl ring contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; or optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S, and

$n$  is independently chosen at each occurrence from 0, 1, and 2.

2. A compound or salt according to Claim 1, wherein:

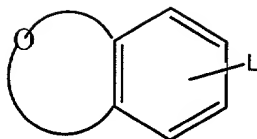
R<sub>3</sub> and R<sub>4</sub> are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R<sub>6</sub>, alkenyl substituted with 0-2 R<sub>6</sub>; alkynyl substituted with 0-2 R<sub>6</sub>; alkoxy substituted with 0-2 R<sub>6</sub>, -NH(alkyl) substituted with 0-2 R<sub>6</sub>, -N(alkyl)(alkyl) where each alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

or any two

R<sub>3</sub> and R<sub>4</sub> not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R<sub>6</sub>, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R<sub>6</sub>, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R<sub>6</sub> and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R<sub>5</sub>; or

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with  $R_5$ , where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

$R_5$  is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2  $R_6$ , alkenyl substituted with 0-2  $R_6$ , alkynyl substituted with 0-2  $R_6$ , alkoxy substituted with 0-2  $R_6$ ,  $-NH(alkyl)$  substituted with 0-2  $R_6$ ,  $-N(alkyl)(alkyl)$  where each alkyl is independently substituted with 0-2  $R_6$ ,  $-XR_7$ , and Y;

$R_6$  is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy,  $-NH(alkyl)$ ,  $-N(alkyl)(alkyl)$ ,  $-S(O)_n(alkyl)$ , haloalkyl, haloalkoxy,  $CO(alkyl)$ ,  $CONH(alkyl)$ ,  $CON(alkyl_1)(alkyl_2)$  where  $alkyl_1$  and  $alkyl_2$  may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S,  $-XR_7$ , and Y;

X is independently selected at each occurrence from the group consisting of  $-CH_2-$ ,  $-CHR_8-$ ,  $-O-$ ,  $-S(O)_n-$ ,  $-NH-$ ,  $-NR_8-$ ,  $-C(=O)-$ ,  $-C(=O)O-$ ,  $-C(=O)NH-$ ,  $-C(=O)NR_8-$ ,  $-S(O)_nNH-$ ,  $-S(O)_nNR_8-$ ,  $NHC(=O)-$ ,  $-NR_8C(=O)-$ ,  $-NHS(O)_n-$ , and  $-NR_8S(O)_n-$ ;

$R_7$  and  $R_8$  are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups

consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)<sub>n</sub>(alkyl), -S(O)<sub>n</sub>(alkyl), -S(O)<sub>n</sub>NH(alkyl), -S(O)<sub>n</sub>N(alkyl<sub>3</sub>)(alkyl<sub>4</sub>) where alkyl<sub>3</sub> and alkyl<sub>4</sub> may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

3. A compound or salt according to Claim 1, wherein: R<sub>A</sub>, R<sub>B</sub>, and R<sub>B</sub>' are independently selected at each occurrence from hydrogen and C<sub>1-6</sub>alkyl; R<sub>3</sub> and R<sub>4</sub> are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>; C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>; C<sub>1-6</sub>alkoxy substituted

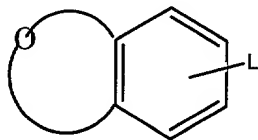
with 0-2  $R_6$ ,  $-NH(C_{1-6}alkyl)$  substituted with 0-2  $R_6$ ,  
 $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$  where each  $C_{1-6}alkyl$  is independently  
substituted with 0-2  $R_6$ ,  
 $-XR_7$ , and Y;

or any two

$R_3$  and  $R_4$  not attached to the same carbon may be joined to form  
an aryl ring substituted with 0-3  $R_6$ , a saturated or  
partially unsaturated carbocyclic ring of from 5 to 8  
members, which carbocyclic ring is substituted with 0-2  $R_6$ ,  
or a saturated, partially unsaturated, or aromatic  
heterocyclic ring of from 5 to 8 members, which  
heterocyclic ring is substituted with 0-2  $R_6$  and contains 1,  
2, or 3 heteroatoms selected from N, O, and S;

$Ar_1$  and  $Ar_2$  may be the same or different and are selected from  
the group consisting of cyclohexyl, cyclopentyl,  
piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl,  
thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl,  
oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl,  
pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl,  
indolyl, isoindolyl, benzofuranyl, isobenzofuranyl,  
benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl,  
isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl,  
each of which is optionally mono-, di-, or trisubstituted  
with  $R_5$ ; or

$Ar_1$  and  $Ar_2$  may be the same or different and represent a bicyclic  
oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with  $R_5$ , where L  
represents point of attachment and may be at any point on  
the benzene ring, and the oxygen-containing ring of the

bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R<sub>5</sub> is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl<sub>1</sub>)(C<sub>1-4</sub>alkyl<sub>2</sub>) where alkyl<sub>1</sub> and alkyl<sub>2</sub> may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR<sub>7</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>8</sub>-, -O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>8</sub>-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR<sub>8</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>8</sub>-, NHC(=O)-, -NR<sub>8</sub>C(=O)-, -NHS(O)<sub>n</sub>-, and -NR<sub>8</sub>S(O)<sub>n</sub>-;

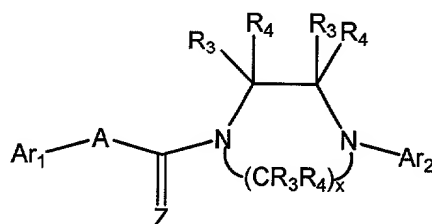
R<sub>7</sub> and R<sub>8</sub> are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy,

-O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl),  
 -NHC(O)(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)C(O)(C<sub>1-4</sub>alkyl), -NHS(O)<sub>n</sub>(C<sub>1-4</sub>alkyl),  
 -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>NH(C<sub>1-4</sub>alkyl),  
 -S(O)<sub>n</sub>N(C<sub>1-4</sub>alkyl)<sub>3</sub>(C<sub>1-4</sub>alkyl)<sub>4</sub> where C<sub>1-4</sub>alkyl<sub>3</sub> and C<sub>1-4</sub>alkyl<sub>4</sub>  
 may be joined to form a heterocycloalkyl ring consisting of  
 from 5 to 8 ring atoms and containing 1, 2, or 3  
 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3-  
 to 8-membered carbocyclic or heterocyclic groups which are  
 saturated, unsaturated, or aromatic, which may be further  
 substituted with one or more substituents independently  
 selected from halogen, oxo, hydroxy, amino, nitro, cyano,  
 C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy,  
 mono- or di(C<sub>1-4</sub>)alkylamino, and C<sub>1-4</sub>alkylthio;  
 wherein said 3- to 8-membered heterocyclic groups contain  
 one or more heteroatom(s) independently selected from N, O,  
 and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

4. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S,

NR<sub>A</sub>, CR<sub>B</sub>R<sub>B'</sub>, NR<sub>A</sub>CR<sub>B</sub>R<sub>B'</sub>,

CR<sub>B</sub>R<sub>B'</sub>NR<sub>A</sub>, -CR<sub>A</sub>=CR<sub>B</sub>-, and C<sub>3</sub>H<sub>4</sub>; where R<sub>A</sub>, R<sub>B</sub>, and R<sub>B'</sub> are



independently selected at each occurrence from hydrogen or alkyl;

Z is oxygen or sulfur;

R<sub>3</sub> and R<sub>4</sub> are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted -S(O)<sub>n</sub>NHalkyl; optionally substituted -S(O)<sub>n</sub>N(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl; optionally substituted -NC(=O)(alkyl)(alkyl); optionally substituted -NHS(O)<sub>n</sub>alkyl; optionally substituted -NS(O)<sub>n</sub>(alkyl)(alkyl); optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

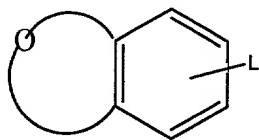
or any two

R<sub>3</sub> and R<sub>4</sub> not attached to the same carbon may be joined to form an optionally substituted aryl ring, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted,

or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidiny, piperaziny, phenyl, pyrroly, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R<sub>5</sub>; or

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R<sub>5</sub>, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R<sub>5</sub> is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl) (C<sub>1-</sub>

alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl<sub>1</sub>)(C<sub>1-4</sub>alkyl<sub>2</sub>) where alkyl<sub>1</sub> and alkyl<sub>2</sub> may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR<sub>7</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>8</sub>-, -O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>8</sub>-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR<sub>8</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>8</sub>-, NHC(=O)-, -NR<sub>8</sub>C(=O)-, -NHS(O)<sub>n</sub>-, and -NR<sub>8</sub>S(O)<sub>n</sub>-;

R<sub>7</sub> and R<sub>8</sub> are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)<sub>n</sub>(alkyl), -S(O)<sub>n</sub>(alkyl), -S(O)<sub>n</sub>NH(alkyl), -S(O)<sub>n</sub>N(alkyl<sub>3</sub>)(alkyl<sub>4</sub>) where alkyl<sub>3</sub> and alkyl<sub>4</sub> may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further

substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S;

n is independently chosen at each occurrence from 0, 1, and 2; and

x is 1 or 3.

5. A compound or salt according to Claim 4, wherein:

R<sub>A</sub>, R<sub>B</sub>, and R<sub>B</sub>' are independently selected at each occurrence from hydrogen or C<sub>1-6</sub>alkyl;

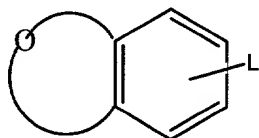
R<sub>3</sub> and R<sub>4</sub> are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>; C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>; C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

or any two

R<sub>3</sub> and R<sub>4</sub> not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R<sub>6</sub>, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R<sub>6</sub>, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R<sub>6</sub> and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidiny, piperaziny, phenyl, pyrroly, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R<sub>5</sub>; or

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R<sub>5</sub>, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R<sub>5</sub> is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy,

-NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl<sub>1</sub>)(C<sub>1-4</sub>alkyl<sub>2</sub>) where alkyl<sub>1</sub> and alkyl<sub>2</sub> may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR<sub>7</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>8</sub>-, -O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>8</sub>-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR<sub>8</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>8</sub>-, NHC(=O)-, -NR<sub>8</sub>C(=O)-, -NHS(O)<sub>n</sub>-, and -NR<sub>8</sub>S(O)<sub>n</sub>-;

R<sub>7</sub> and R<sub>8</sub> are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)C(O)(C<sub>1-4</sub>alkyl), -NHS(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>NH(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>N(C<sub>1-4</sub>alkyl<sub>3</sub>)(C<sub>1-4</sub>alkyl<sub>4</sub>) where C<sub>1-4</sub>alkyl<sub>3</sub> and C<sub>1-4</sub>alkyl<sub>4</sub> may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano,

C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, mono- or di(C<sub>1-4</sub>)alkylamino, and C<sub>1-4</sub>alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S;

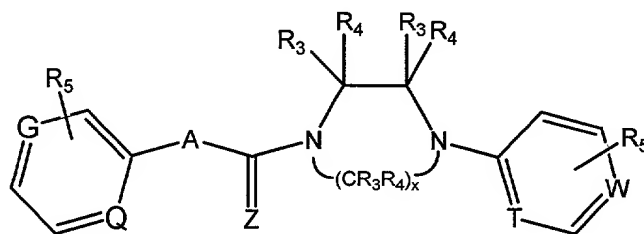
n is independently chosen at each occurrence from 0, 1, and 2;

and

x is 1 or 3.

6. A compound or salt according to Claim 4, wherein Z is oxygen.

7. A compound or salt according to Claim 4 of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

G, Q, T, and W are the same or different and represent N, CH, or CR<sub>5</sub>;

R<sub>A</sub>, R<sub>B</sub>, and R<sub>B</sub>' are independently selected at each occurrence from hydrogen or C<sub>1-6</sub>alkyl;

Z is oxygen or sulfur;

R<sub>3</sub> and R<sub>4</sub> are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally

substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted  $-S(O)_nNHalkyl$ ; optionally substituted  $-S(O)_nN(alkyl)(alkyl)$ ; optionally substituted  $-NHC(=O)alkyl$ ; optionally substituted  $-NC(=O)(alkyl)(alkyl)$ ; optionally substituted  $-NHS(O)_nalkyl$ ; optionally substituted  $-NS(O)_n(alkyl)(alkyl)$ ; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

$R_3$  and  $R_4$  not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

$R_5$  represents 0 to 3 substituents on each of the aryl rings on which it occurs and is independently chosen at each occurrence from the group consisting of halogen, nitro, halo( $C_{1-6}$ )alkyl, halo( $C_{1-6}$ )alkoxy, hydroxy, amino,  $C_{1-6}$ alkyl



substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -NH(alkyl), -N(alkyl)(alkyl), -S(O)<sub>n</sub>(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON(alkyl<sub>1</sub>)(alkyl<sub>2</sub>) where alkyl<sub>1</sub> and alkyl<sub>2</sub> may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR<sub>7</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>8</sub>-, -O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>8</sub>-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR<sub>8</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>8</sub>-, NHC(=O)-, -NR<sub>8</sub>C(=O)-, -NHS(O)<sub>n</sub>-, and -NR<sub>8</sub>S(O)<sub>n</sub>-;

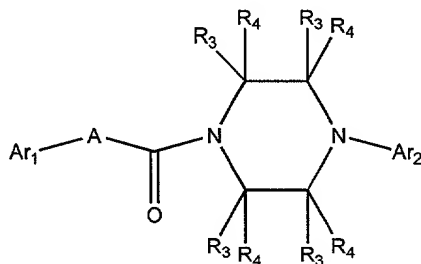
R<sub>7</sub> and R<sub>8</sub> are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)<sub>n</sub>(alkyl), -S(O)<sub>n</sub>(alkyl), -S(O)<sub>n</sub>NH(alkyl), -S(O)<sub>n</sub>N(alkyl<sub>3</sub>)(alkyl<sub>4</sub>) where alkyl<sub>3</sub> and alkyl<sub>4</sub> may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S;

n is independently chosen at each occurrence from 0, 1, and 2; and

x is 1 or 3.

8. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S,  $\text{NR}_A$ ,  $\text{CR}_B\text{R}_B'$ ,  $\text{NR}_A\text{CR}_B\text{R}_B'$ ,  $\text{CR}_B\text{R}_B'\text{NR}_A$ ,  $-\text{CR}_A=\text{CR}_B-$ , and  $\text{C}_3\text{H}_4$ ; where  $\text{R}_A$ ,  $\text{R}_B$ , and  $\text{R}_B'$  are independently selected at each occurrence from hydrogen or alkyl;

$\text{R}_3$  and  $\text{R}_4$  are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro;  $-\text{COOH}$ ;  $-\text{CHO}$ , optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally

substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted  $-S(O)_nNHalkyl$ ; optionally substituted  $-S(O)_nN(alkyl)(alkyl)$ ; optionally substituted  $-NHC(=O)alkyl$ ; optionally substituted  $-NC(=O)(alkyl)(alkyl)$ ; optionally substituted  $-NHS(O)_nalkyl$ ; optionally substituted  $-NS(O)_n(alkyl)(alkyl)$ ; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

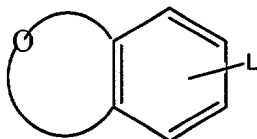
or any two

$R_3$  and  $R_4$  not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

$Ar_1$  and  $Ar_2$  may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidiny, piperaziny, pyrroly, furanyl, thienyl, pyrazoly, imidazoly, thiazoly, isothiazoly, oxazoly,

isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl; wherein Ar<sub>1</sub> is optionally mono-, di-, or trisubstituted with R<sub>5</sub>, and Ar<sub>2</sub> is optionally mono-, di-, or trisubstituted with R<sub>9</sub>; or

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R<sub>5</sub>, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R<sub>5</sub> is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R<sub>6</sub>, alkenyl substituted with 0-2 R<sub>6</sub>, alkynyl substituted with 0-2 R<sub>6</sub>, alkoxy substituted with 0-2 R<sub>6</sub>, -NH(alkyl) substituted with 0-2 R<sub>6</sub>, -N(alkyl)(alkyl) where each alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>9</sub> is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R<sub>6</sub>, alkenyl substituted with 0-2 R<sub>6</sub>, alkynyl substituted with 0-2 R<sub>6</sub>, alkoxy substituted with 0-2 R<sub>6</sub>, -NH(alkyl) substituted with 0-2 R<sub>6</sub>, -N(alkyl)(alkyl)

where each alkyl is independently substituted with 0-2  $R_6$ ,  $-XR_7$ , and Y;

$R_6$  is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy,  $-NH(alkyl)$ ,  $-N(alkyl)(alkyl)$ ,  $-S(O)_n(alkyl)$ , haloalkyl, haloalkoxy,  $CO(alkyl)$ ,  $CONH(alkyl)$ ,  $CON(alkyl_1)(alkyl_2)$  where  $alkyl_1$  and  $alkyl_2$  may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S,  $-XR_7$ , and Y;

X is independently selected at each occurrence from the group consisting of  $-CH_2-$ ,  $-CHR_8-$ ,  $-O-$ ,  $-S(O)_n-$ ,  $-NH-$ ,  $-NR_8-$ ,  $-C(=O)-$ ,  $-C(=O)O-$ ,  $-C(=O)NH-$ ,  $-C(=O)NR_8-$ ,  $-S(O)_nNH-$ ,  $-S(O)_nNR_8-$ ,  $NHC(=O)-$ ,  $-NR_8C(=O)-$ ,  $-NHS(O)_n-$ , and  $-NR_8S(O)_n-$ ;

$R_7$  and  $R_8$  are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy,  $-O(alkyl)$ ,  $-NH(alkyl)$ ,  $-N(alkyl)(alkyl)$ ,  $-NHC(O)(alkyl)$ ,  $-N(alkyl)C(O)(alkyl)$ ,  $-NHS(O)_n(alkyl)$ ,  $-S(O)_n(alkyl)$ ,  $-S(O)_nNH(alkyl)$ ,  $-S(O)_nN(alkyl_3)(alkyl_4)$  where  $alkyl_3$  and  $alkyl_4$  may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and  $Y'$ ;

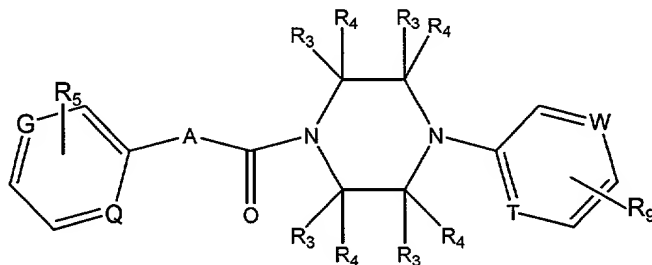
Y and  $Y'$  are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further

substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

9. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

G, Q, T, and W are the same or different and are selected from the group consisting of N, CH, and CR<sub>5</sub>, wherein T or W or both is N;

A is absent or is selected from the group consisting of O, S, NR<sub>A</sub>, CR<sub>B</sub>R<sub>B'</sub>, NR<sub>A</sub>CR<sub>B</sub>R<sub>B'</sub>, CR<sub>B</sub>R<sub>B'</sub>NR<sub>A</sub>, -CR<sub>A</sub>=CR<sub>B</sub>-, and C<sub>3</sub>H<sub>4</sub>; where R<sub>A</sub>, R<sub>B</sub>, and R<sub>B'</sub> are independently selected at each occurrence from hydrogen or alkyl;

Z is oxygen or sulfur;

R<sub>3</sub> and R<sub>4</sub> are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted C<sub>1-6</sub>alkyl; optionally substituted C<sub>2-6</sub>alkenyl; optionally substituted C<sub>2-6</sub>alkynyl; optionally substituted C<sub>1-6</sub>alkoxy; optionally

substituted mono or di(C<sub>1-6</sub>)alkylamino; optionally substituted C<sub>1-6</sub>alkylthio; optionally substituted C<sub>1-6</sub>alkyl ketone; optionally substituted C<sub>1-6</sub>alkylester; optionally substituted C<sub>1-6</sub>alkylsulfinyl; optionally substituted C<sub>1-6</sub>alkylsulfonyl; optionally substituted mono- or di(C<sub>1-6</sub>)alkylcarboxamide; optionally substituted -S(O)<sub>n</sub>NH C<sub>1-6</sub>alkyl; optionally substituted -S(O)<sub>n</sub>N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl); optionally substituted -NHC(=O) C<sub>1-6</sub>alkyl; optionally substituted -NC(=O)(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl); optionally substituted -NHS(O)<sub>n</sub>C<sub>1-6</sub>alkyl; optionally substituted -NS(O)<sub>n</sub>(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl); optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

R<sub>3</sub> and R<sub>4</sub> not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

R<sub>5</sub> represents 1 to 3 substituents and is independently selected at each occurrence from the group consisting of cyano, hydroxy, amino, C<sub>3-6</sub> alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>

alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub> alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>3-6</sub> alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>9</sub> represents 0 to 3 substituents and is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl<sub>1</sub>)(C<sub>1-4</sub>alkyl<sub>2</sub>) where alkyl<sub>1</sub> and alkyl<sub>2</sub> may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR<sub>7</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>8</sub>-, -O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>8</sub>-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR<sub>8</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>8</sub>-, NHC(=O)-, -NR<sub>8</sub>C(=O)-, -NHS(O)<sub>n</sub>-, and -NR<sub>8</sub>S(O)<sub>n</sub>-;

R<sub>7</sub> and R<sub>8</sub> are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more



substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -NHC(O)(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)C(O)(C<sub>1-4</sub>alkyl), -NHS(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>NH(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>N(C<sub>1-4</sub>alkyl)<sub>3</sub>(C<sub>1-4</sub>alkyl)<sub>4</sub> where C<sub>1-4</sub>alkyl<sub>3</sub> and C<sub>1-4</sub>alkyl<sub>4</sub> may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, mono- or di(C<sub>1-4</sub>)alkylamino, and C<sub>1-4</sub>alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and n is independently chosen at each occurrence from 0, 1, and 2.

10. A compound according to Claim 9, which is 4-(3-Chloro-2-pyridinyl)-N-[4(isopropyl)phenyl]-2-methylthio-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

11. A compound according to Claim 9, wherein R<sub>3</sub> and R<sub>4</sub> are independently selected at each occurrence from the group consisting of hydrogen and C<sub>1-6</sub> alkyl.

12. A compound according to Claim 11, wherein G and Q are selected from the group consisting of CH and CR<sub>5</sub>.

13. A compound according to Claim 11, wherein G , Q, and W are independently selected at each occurrence from the group consisting of CH and CR<sub>5</sub>; and T is N.

14. A compound according to Claim 13 wherein R<sub>3</sub> and R<sub>4</sub> are hydrogen; and A is selected from the group consisting of NH, -CH=CH-, and -CH<sub>2</sub>NH-.

15. A compound or salt according to Claim 14, wherein R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, -NH(C<sub>1-4</sub>alkyl), and -N(C<sub>1-4</sub> alkyl)(C<sub>1-4</sub> alkyl).

16. A compound according to Claim 14, which is 4-(3-Trifluoromethyl-2-pyridinyl)-N-(3-methoxy-4-hydroxyphenylmethyl)-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

17. A compound according to Claim 14, which is 4-(3-Nitro-2-pyridinyl)-N-[4-(n-butyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

18. A compound according to Claim 14, which is 4-(3-Trifluoromethyl-2-pyridinyl)-N-[4-(n-butyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

19. A compound according to Claim 14, which is 4-(3-Methyl-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

20. A compound according to Claim 14, which is 4-(3-Methyl-2-pyridinyl)-N-[4-(n-butyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

21. A compound according to Claim 14, which is 4-(3-Chloro-5-trifluoromethyl-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

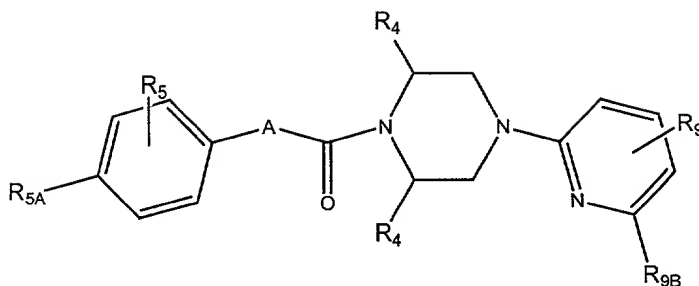
22. A compound according to Claim 14, which is 4-(3-Chloro-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

23. A compound according to Claim 14, which is 4-(3,5-Dichloro-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

24. A compound according to claim 13, which is 4-(3-Cyano-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

25. The compound according to claim 13, which is 4-(3-Chloro-2-pyridinyl)-N-[4-(isopropyl)phenyl]-2-methyl-1-piperazinecarboxamide.

26. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH<sub>2</sub>NH;

R<sub>4</sub> is independently chosen from hydrogen and C<sub>1-4</sub> alkyl;

R<sub>5</sub> represents 0 to 2 substituents and is independently chosen at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub> alkyl is independently substituted with 0-2 R<sub>6</sub>;

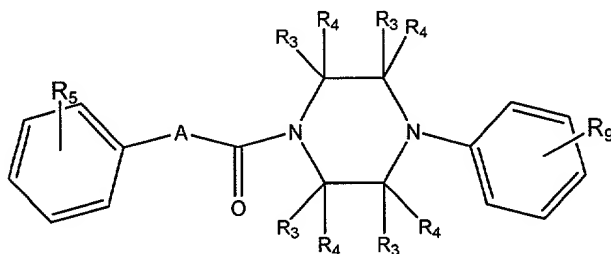
R<sub>9</sub> represents 0 to 2 substituents and is independently chosen at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>;

R<sub>5A</sub> is independently selected from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, -NH(C<sub>1-6</sub> alkyl), and -N(C<sub>1-6</sub> alkyl)(C<sub>1-6</sub> alkyl);

$R_{9B}$  is independently selected from the group consisting of halogen, nitro, halo( $C_{1-6}$ )alkoxy, hydroxy, amino,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $-NH(C_{1-6}$  alkyl), and  $-N(C_{1-6}$  alkyl)( $C_{1-6}$  alkyl); and

$R_6$  is independently selected at each occurrence the group consisting of halogen, hydroxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $-NH(C_{1-4}$  alkyl), and  $-N(C_{1-4}$  alkyl)( $C_{1-4}$  alkyl).

27. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of a single bond, S,  $NR_A$ ,  $CHR_B$ ,  $NR_ACHR_B$ ,  $CHR_BNR_A$ ,  $-CR_A=CR_B-$ , and  $C_3H_4$ ; where  $R_A$  and  $R_B$  are independently selected at each occurrence from the group consisting of hydrogen and alkyl;

$R_3$  and  $R_4$  are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro;  $-COOH$ ;  $-CHO$ , optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted  $-S(O)_nNHalkyl$ ; optionally substituted  $-S(O)_nN(alkyl)(alkyl)$ ; optionally substituted  $-NHC(=O)alkyl$ ;

optionally substituted  $\text{-NC(=O)(alkyl)(alkyl)}$ ; optionally substituted  $\text{-NHS(O)}_n\text{alkyl}$ ; optionally substituted  $\text{-NS(O)}_n\text{(alkyl)(alkyl)}$ ; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

$R_3$  and  $R_4$  not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

$R_5$  is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy,  $C_{1-6}$  alkyl substituted with 0-2  $R_6$ ,  $C_{2-6}$  alkenyl substituted with 0-2  $R_6$ ,  $C_{2-6}$  alkynyl substituted with 0-2  $R_6$ ,  $C_{1-6}$  alkoxy substituted with 0-2  $R_6$ ,  $\text{-NH}(C_{1-6} \text{ alkyl})$  substituted with 0-2  $R_6$ ,  $\text{-N}(C_{1-6} \text{ alkyl})(C_{1-6} \text{ alkyl})$  where each alkyl is independently substituted with 0-2  $R_6$ ,  $\text{-XR}_7$ , and Y;

$R_9$  represents 0-3 substituents and is independently selected at each occurrence from the group consisting of bromo, haloalkyl, haloalkoxy, hydroxy,  $C_{2-6}$  alkyl substituted with 0-2  $R_6$ ,  $C_{2-6}$  alkenyl substituted with 0-2  $R_6$ ,  $C_{2-6}$  alkynyl

substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub> alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>2-6</sub> alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>2-6</sub> alkyl)(C<sub>2-6</sub> alkyl) where each C<sub>2-6</sub> alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -NH(alkyl), -N(alkyl)(alkyl), -S(O)<sub>n</sub>(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON(alkyl<sub>1</sub>)(alkyl<sub>2</sub>) where alkyl<sub>1</sub> and alkyl<sub>2</sub> may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR<sub>7</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>8</sub>-, -O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>8</sub>-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR<sub>8</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>8</sub>-, NHC(=O)-, -NR<sub>8</sub>C(=O)-, -NHS(O)<sub>n</sub>-, and -NR<sub>8</sub>S(O)<sub>n</sub>-;

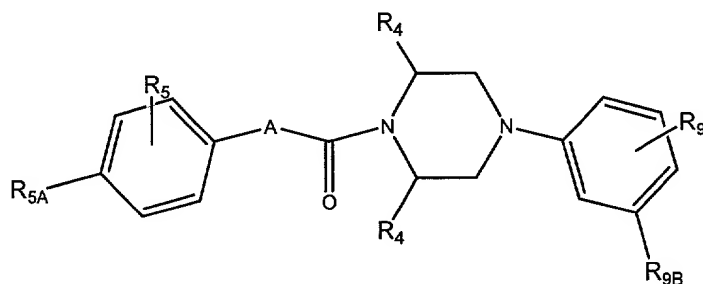
R<sub>7</sub> and R<sub>8</sub> are independently selected at each occurrence from straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 3 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 3 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)<sub>n</sub>(alkyl), -S(O)<sub>n</sub>(alkyl), -S(O)<sub>n</sub>NH(alkyl), -S(O)<sub>n</sub>N(alkyl<sub>3</sub>)(alkyl<sub>4</sub>) where alkyl<sub>3</sub> and alkyl<sub>4</sub> may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and n is independently chosen at each occurrence from 0, 1, and 2.

28. A compound or salt according to Claim 27 in which R<sub>3</sub> and R<sub>4</sub> are independently selected at each occurrence from the group consisting of hydrogen and C<sub>1-6</sub> alkyl.

29. A compound or salt according to claim 27, wherein A is selected from the group consisting of NH, -CH=CH-, and CH<sub>2</sub>NH; R<sub>3</sub> is hydrogen and R<sub>4</sub> is independently chosen at each occurrence from hydrogen and methyl; and R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, -NH(C<sub>1-4</sub> alkyl), and -N(C<sub>1-4</sub> alkyl)(C<sub>1-4</sub> alkyl).

30. A compound of the formula:





or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH<sub>2</sub>NH;

R<sub>4</sub> is independently selected at each occurrence from hydrogen and C<sub>1-4</sub>alkyl;

R<sub>5</sub> represents 0 to 2 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>;

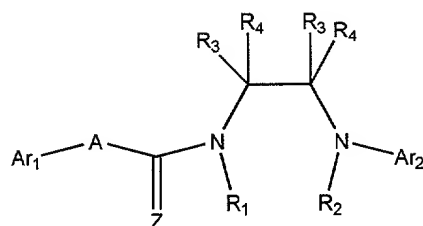
R<sub>9</sub> represents 0 to 2 substituents and is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>;

R<sub>5A</sub> is independently selected from the group consisting of halogen, cyano, nitro, trifluoromethyl, trifluoromethoxy, hydroxy, amino, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, -NH(C<sub>1-6</sub> alkyl), and -N(C<sub>1-6</sub> alkyl)(C<sub>1-6</sub> alkyl);

R<sub>9B</sub> is independently selected from the group consisting of trifluoromethoxy, hydroxy, C<sub>2-6</sub> alkyl, C<sub>2-6</sub> alkoxy, -NH(C<sub>2-6</sub> alkyl), and -N(C<sub>2-6</sub> alkyl)(C<sub>2-6</sub> alkyl); and

R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, -NH(C<sub>1-4</sub> alkyl), and -N(C<sub>1-4</sub> alkyl)(C<sub>1-4</sub> alkyl).

31. A compound of the formula:



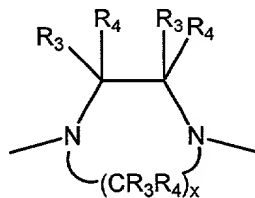
or a pharmaceutically acceptable salt thereof, wherein the compound or pharmaceutically acceptable salt thereof exhibits an EC<sub>50</sub> or K<sub>i</sub> of 1 micromolar or less in a standard assay of capsaicin receptor mediated calcium mobilization; and wherein

A is absent or is selected from the group consisting of O, S, NR<sub>A</sub>, CR<sub>B</sub>R<sub>B'</sub>, NR<sub>A</sub>CR<sub>B</sub>R<sub>B'</sub>, CR<sub>B</sub>R<sub>B'</sub>NR<sub>A</sub>, -CR<sub>A</sub>=CR<sub>B</sub>-, and C<sub>3</sub>H<sub>4</sub>; where R<sub>A</sub>, R<sub>B</sub>, and R<sub>B'</sub> are independently selected at each occurrence from hydrogen or C<sub>1-6</sub> alkyl;

Z is oxygen or sulfur;

R<sub>1</sub> and R<sub>2</sub> independently represent hydrogen or C<sub>1-6</sub> alkyl; or

R<sub>1</sub> and R<sub>2</sub> are taken together to form a 5 to 8 membered nitrogen-containing ring of the formula:



wherein x is 1, 2, or 3;

R<sub>3</sub> and R<sub>4</sub> are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>;

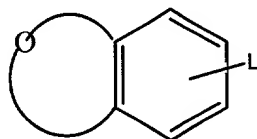
C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>; C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

or any two

R<sub>3</sub> and R<sub>4</sub> not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R<sub>6</sub>, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R<sub>6</sub>, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R<sub>6</sub> and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R<sub>5</sub>; or

Ar<sub>1</sub> and Ar<sub>2</sub> may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R<sub>5</sub>, where L represents point of attachment and may be at any point on

the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R<sub>5</sub> is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl<sub>1</sub>)(C<sub>1-4</sub>alkyl<sub>2</sub>) where alkyl<sub>1</sub> and alkyl<sub>2</sub> may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR<sub>7</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>8</sub>-, -O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>8</sub>-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR<sub>8</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>8</sub>-, NHC(=O)-, -NR<sub>8</sub>C(=O)-, -NHS(O)<sub>n</sub>-, and -NR<sub>8</sub>S(O)<sub>n</sub>-;

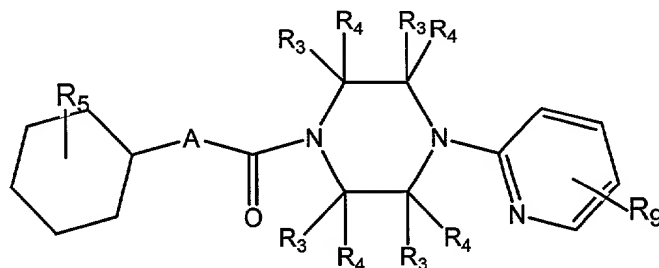
R<sub>7</sub> and R<sub>8</sub> are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy,

halogen, amino, cyano, nitro, haloalkyl, haloalkoxy,  $-O(C_{1-4}alkyl)$ ,  
 $-NH(C_{1-4}alkyl)$ ,  $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$ ,  $-NHC(O)(C_{1-4}alkyl)$ ,  $-$   
 $N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl)$ ,  $-NHS(O)_n(C_{1-4}alkyl)$ ,  $-S(O)_n(C_{1-4}alkyl)$ ,  
 $-S(O)_nNH(C_{1-4}alkyl)$ ,  
 $-S(O)_nN(C_{1-4}alkyl_3)(C_{1-4}alkyl_4)$  where  $C_{1-4}alkyl_3$  and  $C_{1-4}alkyl_4$   
 may be joined to form a heterocycloalkyl ring consisting of  
 from 5 to 8 ring atoms and containing 1, 2, or 3  
 heteroatoms selected from N, O, and S, and Y' ;

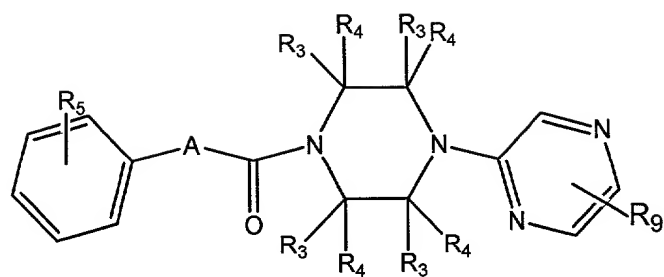
Y and Y' are independently selected at each occurrence from 3-  
 to 8-membered carbocyclic or heterocyclic groups which are  
 saturated, unsaturated, or aromatic, which may be further  
 substituted with one or more substituents independently  
 selected from halogen, oxo, hydroxy, amino, nitro, cyano,  
 $C_{1-4}alkyl$ ,  $C_{1-4}alkoxy$ , halo( $C_{1-4}$ )alkyl, halo( $C_{1-4}$ )alkoxy,  
 mono- or di( $C_{1-4}$ )alkylamino, and  $C_{1-4}alkylthio$ ;  
 wherein said 3- to 8-membered heterocyclic groups contain  
 one or more heteroatom(s) independently selected from N, O,  
 and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

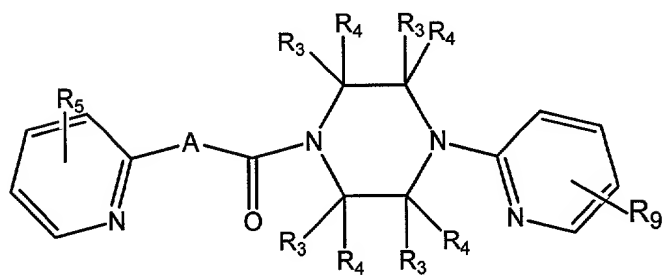
32. A compound of the Formula A, Formula B, Formula C,  
 Formula D, Formula E, or Formula F:



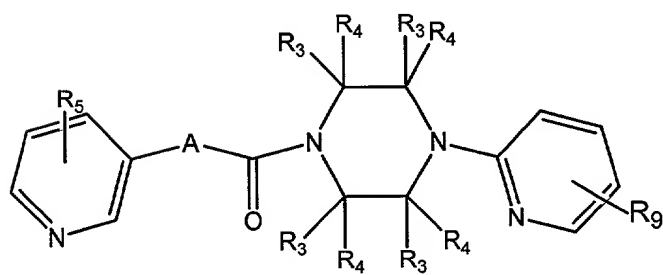
**Formula A**



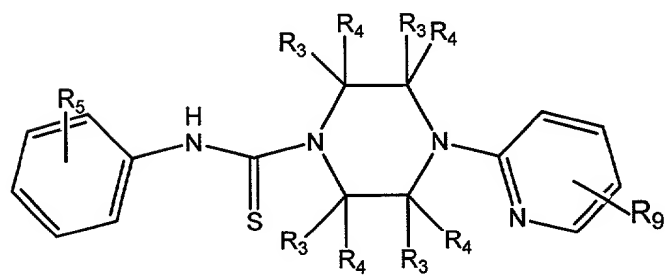
**Formula B**



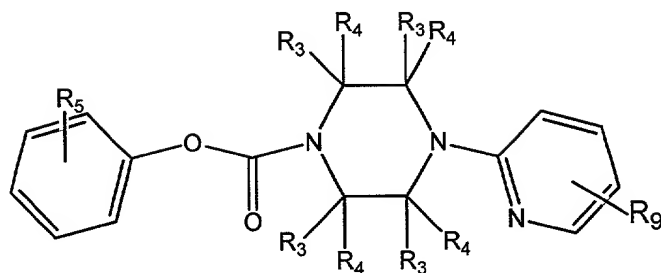
**Formula C**



**Formula D**



# Formula E



# Formula F

or a pharmaceutically acceptable salt of Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F, wherein A represents NH or O;

R<sub>3</sub> and R<sub>4</sub> are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>; C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>; C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, -XR<sub>7</sub>, and Y;

or any two

R<sub>3</sub> and R<sub>4</sub> not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R<sub>6</sub>, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R<sub>6</sub>, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which

heterocyclic ring is substituted with 0-2  $R_6$  and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

$R_5$  and  $R_9$  each represent from 1 to 3 substituents and are independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo( $C_{1-6}$ )alkyl, halo( $C_{1-6}$ )alkoxy, hydroxy, amino,  $C_{1-6}$ alkyl substituted with 0-2  $R_6$ ,  $C_{2-6}$ alkenyl substituted with 0-2  $R_6$ ,  $C_{2-6}$ alkynyl substituted with 0-2  $R_6$ ,  $C_{1-6}$ alkoxy substituted with 0-2  $R_6$ ,  $-NH(C_{1-6}alkyl)$  substituted with 0-2  $R_6$ ,  $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$  where each  $C_{1-6}alkyl$  is independently substituted with 0-2  $R_6$ ,  $-XR_7$ , and Y;

$R_6$  is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano,  $C_{1-4}alkyl$ ,  $C_{1-4}alkoxy$ ,  $-NH(C_{1-4}alkyl)$ ,  $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$ ,  $-S(O)_n(C_{1-4}alkyl)$ , halo( $C_{1-4}$ )alkyl, halo( $C_{1-4}$ )alkoxy,  $CO(C_{1-4}alkyl)$ ,  $CONH(C_{1-4}alkyl)$ ,  $CON(C_{1-4}alkyl_1)(C_{1-4}alkyl_2)$  where  $alkyl_1$  and  $alkyl_2$  may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S,  $-XR_7$ , and Y;

X is independently selected at each occurrence from the group consisting of  $-CH_2-$ ,  $-CHR_8-$ ,  $-O-$ ,  $-S(O)_n-$ ,  $-NH-$ ,  $-NR_8-$ ,  $-C(=O)-$ ,  $-C(=O)O-$ ,  $-C(=O)NH-$ ,  $-C(=O)NR_8-$ ,  $-S(O)_nNH-$ ,  $-S(O)_nNR_8-$ ,  $NHC(=O)-$ ,  $-NR_8C(=O)-$ ,  $-NHS(O)_n-$ , and  $-NR_8S(O)_n-$ ;

$R_7$  and  $R_8$  are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy,  $-O(C_{1-}$



$\text{C}_{1-4}\text{alkyl}$ ),  $-\text{NH}(\text{C}_{1-4}\text{alkyl})$ ,  $-\text{N}(\text{C}_{1-4}\text{alkyl})(\text{C}_{1-4}\text{alkyl})$ ,  
 $-\text{NHC}(\text{O})(\text{C}_{1-4}\text{alkyl})$ ,  $-\text{N}(\text{C}_{1-4}\text{alkyl})\text{C}(\text{O})(\text{C}_{1-4}\text{alkyl})$ ,  
 $-\text{NHS}(\text{O})_n(\text{C}_{1-4}\text{alkyl})$ ,  $-\text{S}(\text{O})_n(\text{C}_{1-4}\text{alkyl})$ ,  $-\text{S}(\text{O})_n\text{NH}(\text{C}_{1-4}\text{alkyl})$ ,  $-\text{S}(\text{O})_n\text{N}(\text{C}_{1-4}\text{alkyl}_3)(\text{C}_{1-4}\text{alkyl}_4)$  where  $\text{C}_{1-4}\text{alkyl}_3$  and  $\text{C}_{1-4}\text{alkyl}_4$  may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano,  $\text{C}_{1-4}\text{alkyl}$ ,  $\text{C}_{1-4}\text{alkoxy}$ ,  $\text{halo}(\text{C}_{1-4})\text{alkyl}$ ,  $\text{halo}(\text{C}_{1-4})\text{alkoxy}$ , mono- or di( $\text{C}_{1-4}$ )alkylamino, and  $\text{C}_{1-4}\text{alkylthio}$ ; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and  
 n is independently chosen at each occurrence from 0, 1, and 2.

33. A compound or salt according to Claim 32, wherein A represents NH.

34. A compound or salt according to Claim 32, wherein:  
 A represents NH; and  
 $\text{R}_3$  and  $\text{R}_4$  are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro,  $\text{halo}(\text{C}_{1-6})\text{alkyl}$ ,  $\text{halo}(\text{C}_{1-6})\text{alkoxy}$ , hydroxy, amino,  $\text{C}_{1-6}\text{alkyl}$ ,  $\text{C}_{2-6}\text{alkenyl}$ ,  $\text{C}_{2-6}\text{alkynyl}$ ,  $\text{C}_{1-6}\text{alkoxy}$  substituted with 0-2  $\text{R}_6$ ,  $-\text{NH}(\text{C}_{1-6}\text{alkyl})$ , and  $-\text{N}(\text{C}_{1-6}\text{alkyl})(\text{C}_{1-6}\text{alkyl})$ .

35. A compound or salt according to Claim 32, wherein:  
 A represents NH;

R<sub>3</sub> represents hydrogen; and

R<sub>4</sub> is independently chosen at each occurrence from hydrogen and C<sub>1-6</sub> alkyl.

36. A compound or salt according to Claim 32, wherein:

A represents NH;

R<sub>3</sub> represents hydrogen; and

R<sub>4</sub> is independently chosen at each occurrence from hydrogen and methyl.

37. A compound or salt according to Claim 32, wherein:

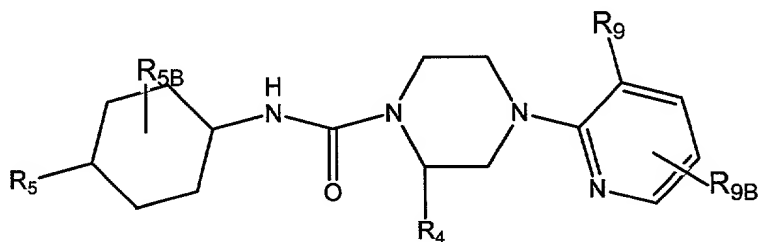
A represents NH;

R<sub>3</sub> represents hydrogen;

R<sub>4</sub> is independently chosen at each occurrence from hydrogen and methyl; and

R<sub>5</sub> and R<sub>9</sub> each represent from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and C<sub>3-8</sub> cycloalkyl.

38. A compound or salt according to Claim 37 of the Formula A-1



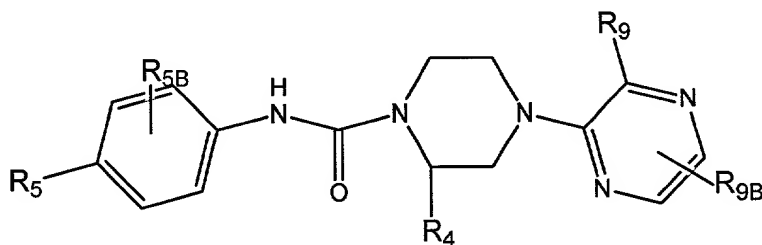
**Formula A-1**

R<sub>5</sub> and R<sub>9</sub> are independently selected from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and C<sub>3-8</sub> cycloalkyl; and

R<sub>5B</sub> and R<sub>9B</sub> each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, hydroxy, amino, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, -NH(C<sub>1-3</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl).

39. A compound or salt according to Claim 38, wherein:  
R<sub>5</sub> is C<sub>3-6</sub> alkyl; C<sub>3-6</sub> alkoxy; halo(C<sub>1-3</sub>)alkyl, halo(C<sub>1-3</sub>)alkoxy, or C<sub>3-8</sub> cycloalkyl;  
R<sub>9</sub> is chloro or trifluoromethyl; and  
R<sub>5B</sub> and R<sub>9B</sub> are hydrogen.

40. A compound or salt according to Claim 37 of Formula B-1



**Formula B-1**

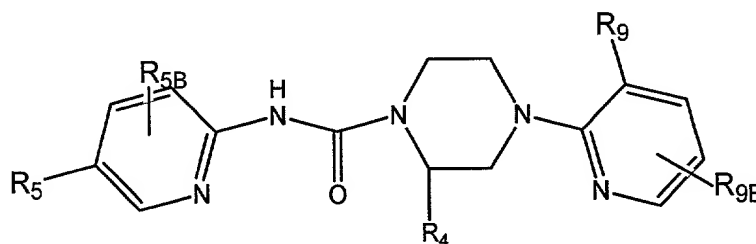
wherein

R<sub>5</sub> and R<sub>9</sub> are independently selected from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and C<sub>3-8</sub> cycloalkyl; and

R<sub>5B</sub> and R<sub>9B</sub> each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, hydroxy, amino, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, -NH(C<sub>1-3</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl).

41. A compound or salt according to Claim 40, wherein:  
 R<sub>5</sub> is C<sub>3-6</sub> alkyl; C<sub>3-6</sub> alkoxy; halo(C<sub>1-3</sub>)alkyl, halo(C<sub>1-3</sub>)alkoxy, or C<sub>3-8</sub> cycloalkyl;  
 R<sub>9</sub> is chloro or trifluoromethyl; and  
 R<sub>5B</sub> and R<sub>9B</sub> are hydrogen.

42. A compound or salt according to Claim 37 of Formula C-1:



**Formula C-1**

wherein:

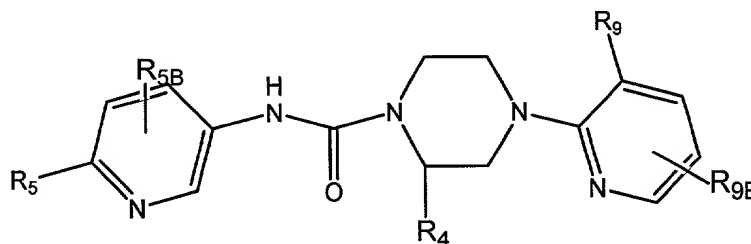
R<sub>5</sub> and R<sub>9</sub> are independently selected from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and C<sub>3-8</sub> cycloalkyl; and

R<sub>5B</sub> and R<sub>9B</sub> each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, hydroxy, amino,

C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, -NH(C<sub>1-3</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl).

43. A compound or salt according to Claim 42, wherein:  
R<sub>5</sub> is C<sub>3-6</sub> alkyl; C<sub>3-6</sub> alkoxy; halo(C<sub>1-3</sub>)alkyl, halo(C<sub>1-3</sub>)alkoxy, or C<sub>3-8</sub> cycloalkyl;  
R<sub>9</sub> is chloro or trifluoromethyl; and  
R<sub>5B</sub> and R<sub>9B</sub> are hydrogen.

44. A compound or salt according to Claim 37 of Formula D-1



**Formula D-1**

wherein:

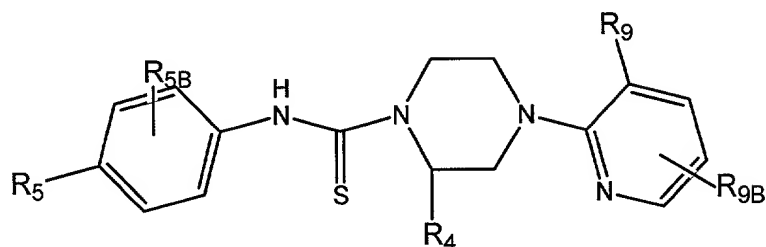
R<sub>5</sub> and R<sub>9</sub> are independently selected from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and C<sub>3-8</sub> cycloalkyl; and

R<sub>5B</sub> and R<sub>9B</sub> each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, hydroxy, amino, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, -NH(C<sub>1-3</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl).

45. A compound or salt according to Claim 44, wherein:  
R<sub>5</sub> is C<sub>3-6</sub> alkyl; C<sub>3-6</sub> alkoxy; halo(C<sub>1-3</sub>)alkyl, halo(C<sub>1-3</sub>)alkoxy, or C<sub>3-8</sub> cycloalkyl;

R<sub>9</sub> is chloro or trifluoromethyl; and  
 R<sub>5B</sub> and R<sub>9B</sub> are hydrogen.

46. A compound or salt according to Claim 37, of Formula E-1



**Formula E-1**

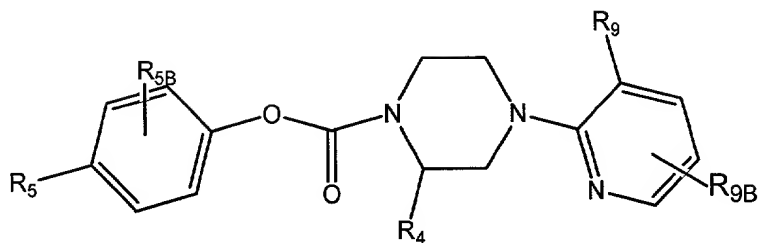
wherein:

R<sub>5</sub> and R<sub>9</sub> are independently selected from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and C<sub>3-8</sub> cycloalkyl; and

R<sub>5B</sub> and R<sub>9B</sub> each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, hydroxy, amino, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, -NH(C<sub>1-3</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl).

47. A compound or salt according to Claim 46, wherein:  
 R<sub>5</sub> is C<sub>3-6</sub> alkyl; C<sub>3-6</sub> alkoxy; halo(C<sub>1-3</sub>)alkyl, halo(C<sub>1-3</sub>)alkoxy, or C<sub>3-8</sub> cycloalkyl;  
 R<sub>9</sub> is chloro or trifluoromethyl; and  
 R<sub>5B</sub> and R<sub>9B</sub> are hydrogen.

48. A compound of salt according to Claim 37 of Formula F-1



**Formula F-1**

wherein:

R<sub>5</sub> and R<sub>9</sub> are independently selected from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and C<sub>3-8</sub>cycloalkyl; and

R<sub>5B</sub> and R<sub>9B</sub> each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, hydroxy, amino, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, -NH(C<sub>1-3</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl).

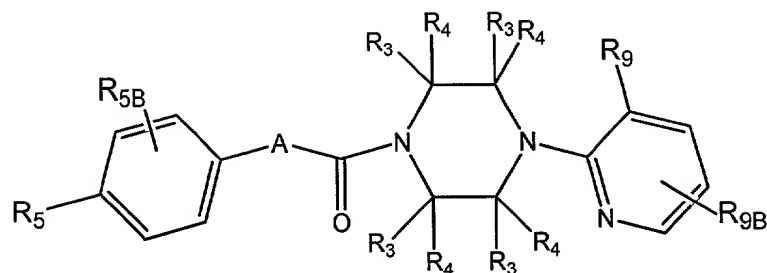
49. A compound or salt according to Claim 47, wherein:

R<sub>5</sub> is C<sub>3-6</sub> alkyl; C<sub>3-6</sub> alkoxy; halo(C<sub>1-3</sub>)alkyl, halo(C<sub>1-3</sub>)alkoxy, or C<sub>3-8</sub> cycloalkyl;

R<sub>9</sub> is chloro or trifluoromethyl; and

R<sub>5B</sub> and R<sub>9B</sub> are hydrogen.

50. A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S,  $\text{NR}_A$ ,  $\text{CR}_B\text{R}_B'$ ,  $\text{NR}_A\text{CR}_B\text{R}_B'$ ,  $\text{CR}_B\text{R}_B'\text{NR}_A$ ,  $-\text{CR}_A=\text{CR}_B-$ , and  $\text{C}_3\text{H}_4$ ; where  $\text{R}_A$ ,  $\text{R}_B$ , and  $\text{R}_B'$  are independently selected at each occurrence from hydrogen or  $\text{C}_{1-6}$  alkyl;

$\text{R}_3$  and  $\text{R}_4$  are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo( $\text{C}_{1-6}$ )alkyl, halo( $\text{C}_{1-6}$ )alkoxy, hydroxy, amino,  $\text{C}_{1-6}$ alkyl substituted with 0-2  $\text{R}_6$ ,  $\text{C}_{2-6}$ alkenyl substituted with 0-2  $\text{R}_6$ ;  $\text{C}_{2-6}$ alkynyl substituted with 0-2  $\text{R}_6$ ;  $\text{C}_{1-6}$ alkoxy substituted with 0-2  $\text{R}_6$ ,  $-\text{NH}(\text{C}_{1-6}\text{alkyl})$  substituted with 0-2  $\text{R}_6$ ,  $-\text{N}(\text{C}_{1-6}\text{alkyl})(\text{C}_{1-6}\text{alkyl})$  where each  $\text{C}_{1-6}\text{alkyl}$  is independently substituted with 0-2  $\text{R}_6$ ,  $-\text{XR}_7$ , and Y;

or any two

$\text{R}_3$  and  $\text{R}_4$  not attached to the same carbon may be joined to form an aryl ring substituted with 0-3  $\text{R}_6$ , a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2  $\text{R}_6$ , or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2  $\text{R}_6$  and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

$\text{R}_5$  is selected from the group consisting of bromo, fluoro, iodo, halo( $\text{C}_{1-6}$ )alkyl, halo( $\text{C}_{3-6}$ )alkoxy,  $\text{C}_{3-6}$ alkyl substituted with



0-3 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-3 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-3 R<sub>6</sub>, C<sub>3-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, (C<sub>3-8</sub>cycloalkyl)C<sub>1-4</sub>alkyl, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is substituted with 0-2 R<sub>6</sub>, Y, -(C=O)Y, -(CH<sub>2</sub>)Y, and -(CH(CN))Y;

R<sub>9</sub> is selected from the group consisting of halogen, cyano, -N(SO<sub>2</sub>C<sub>1-6</sub>alkyl)(SO<sub>2</sub>C<sub>1-6</sub>alkyl), -SO<sub>2</sub>NH<sub>2</sub>, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is substituted with 0-2 R<sub>6</sub>;

R<sub>5B</sub> and R<sub>9B</sub> each represent from 0 to 2 substituents and are independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>6</sub>, (C<sub>3-8</sub>cycloalkyl)C<sub>1-4</sub>alkyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>6</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>6</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>6</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>6</sub>, and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) where each C<sub>1-6</sub>alkyl is independently substituted with 0-2 R<sub>6</sub>, and Y; and any two

R<sub>5</sub> and R<sub>5B</sub> bound to adjacent atoms may be joined to form a C<sub>3-8</sub>cycloalkyl group or a heterocycloalkyl group, each of which is optionally substituted by from 1 to 5 substituents independently chosen from cyano, halogen, hydroxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), halo(C<sub>1-4</sub>)alkyl, and halo(C<sub>1-4</sub>)alkoxy, wherein the heterocycloalkyl group consists of from 4 to 8 atoms and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl<sub>1</sub>)(C<sub>1-4</sub>alkyl<sub>2</sub>) where alkyl<sub>1</sub> and alkyl<sub>2</sub> may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR<sub>7</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>8</sub>-, -O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>8</sub>-, -C(=O)-, -C(=O)NH-, -C(=O)NR<sub>8</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>8</sub>-, NHC(=O)-, -NR<sub>8</sub>C(=O)-, -NHS(O)<sub>n</sub>-, and -NR<sub>8</sub>S(O)<sub>n</sub>-;

R<sub>7</sub> and R<sub>8</sub> are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -NHC(O)(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)C(O)(C<sub>1-4</sub>alkyl), -NHS(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>NH(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>N(C<sub>1-4</sub>alkyl<sub>3</sub>)(C<sub>1-4</sub>alkyl<sub>4</sub>) where C<sub>1-4</sub>alkyl<sub>3</sub> and C<sub>1-4</sub>alkyl<sub>4</sub> may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently

selected from halogen, oxo, hydroxy, amino, nitro, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, mono- or di(C<sub>1-4</sub>)alkylamino, and C<sub>1-4</sub>alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

51. A compound or salt according to Claim 50, wherein:  
A is O or NR<sub>A</sub>, wherein R<sub>A</sub> is hydrogen or methyl.

52. A compound or salt according to Claim 50, wherein:  
A is O or NR<sub>A</sub>, wherein R<sub>A</sub> is hydrogen or methyl; and  
R<sub>3</sub> and R<sub>4</sub> are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl).

53. A compound or salt according to Claim 50, wherein:  
A is O or NR<sub>A</sub>, wherein R<sub>A</sub> is hydrogen or methyl;  
R<sub>3</sub> is hydrogen; and  
R<sub>4</sub> is independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl).

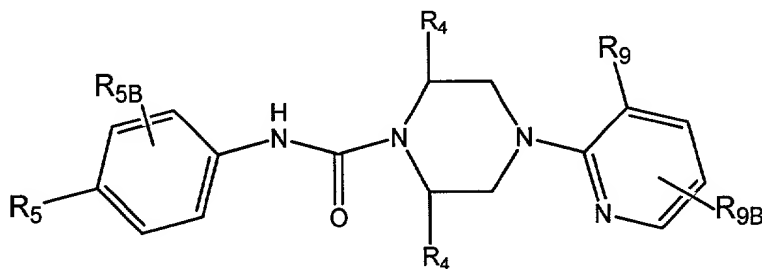
54. A compound or salt according to Claim 50, wherein:  
A is O or NR<sub>A</sub>, wherein R<sub>A</sub> is hydrogen or methyl;  
R<sub>3</sub> is hydrogen; and

R<sub>4</sub> is independently chosen at each occurrence from hydrogen and C<sub>1-6</sub>alkyl.

55. A compound or salt according to Claim 50, wherein:  
A is NR<sub>A</sub>, wherein R<sub>A</sub> is hydrogen or methyl;  
R<sub>3</sub> is hydrogen; and  
R<sub>4</sub> is independently chosen at each occurrence from hydrogen, halo(C<sub>1-3</sub>)alkyl, and C<sub>1-6</sub>alkyl.

56. A compound or salt according to Claim 50, wherein:  
A is NR<sub>A</sub>, wherein R<sub>A</sub> is hydrogen or methyl;  
R<sub>3</sub> is hydrogen; and  
R<sub>4</sub> is independently chosen at each occurrence from hydrogen and C<sub>1-4</sub>alkyl.

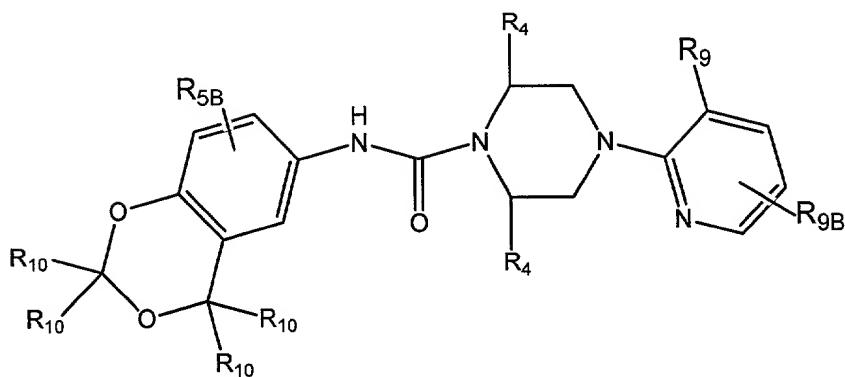
57. A compound or salt according to Claim 50 of the Formula



wherein:

R<sub>4</sub> is independently chosen at each occurrence from hydrogen and C<sub>1-4</sub>alkyl.

58. A compound or salt according to Claim 57 of the formula:



wherein

$R_{5B}$  and  $R_{9B}$  are independently chosen from hydrogen, halogen, cyano, nitro, halo( $C_{1-2}$ )alkyl, halo( $C_{1-2}$ )alkoxy, amino,  $C_{1-4}$ alkyl, and  $C_{1-2}$ alkoxy; and

$R_{10}$  is independently chosen at each occurrence from hydrogen, halogen, and  $C_{1-4}$  alkyl.

59. A compound or salt according to Claim 58 wherein:  
 $R_9$  is selected from the group consisting of halogen, cyano,  $-N(SO_2CH_3)_2$ ,  $-SO_2NH_2$ , halo( $C_{1-3}$ )alkyl,  $C_{1-3}$ alkoxy,  $-NH(C_{1-3}alkyl)$ , and  $-N(C_{1-3}alkyl)(C_{1-3}alkyl)$ .

60. A compound or salt according to Claim 57, wherein:  
 $R_{5B}$  and  $R_{9B}$  are independently chosen from hydrogen, halogen, cyano, nitro, halo( $C_{1-2}$ )alkyl, halo( $C_{1-2}$ )alkoxy, amino,  $C_{1-4}$ alkyl, and  $C_{1-2}$ alkoxy.

61. A compound or salt according to Claim 57, wherein:  
 $R_{5B}$  represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo( $C_{1-2}$ )alkyl, halo( $C_{1-2}$ )alkoxy, amino,  $C_{1-4}$ alkyl, and  $C_{1-2}$ alkoxy; and  
 $R_{9B}$  represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo( $C_{1-2}$ )alkyl, and  $C_{1-2}$ alkyl, and  $C_{1-2}$ alkoxy.

62. A compound or salt according to Claim 57, wherein:

R<sub>9</sub> is selected from the group consisting of halogen, cyano, -N(SO<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>, -SO<sub>2</sub>NH<sub>2</sub>, halo(C<sub>1-3</sub>)alkyl, C<sub>1-3</sub>alkoxy, -NH(C<sub>1-3</sub>alkyl), and -N(C<sub>1-3</sub>alkyl)(C<sub>1-3</sub>alkyl);

R<sub>5B</sub> represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, amino, C<sub>1-4</sub>alkyl, and C<sub>1-2</sub>alkoxy; and

R<sub>9B</sub> represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, and C<sub>1-2</sub>alkyl, and C<sub>1-2</sub>alkoxy.

63. A compound or salt according to Claim 57, wherein:

R<sub>5</sub> is selected from the group consisting of bromo, fluoro, iodo, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>3-6</sub>)alkoxy, C<sub>3-6</sub>alkyl substituted with 0-3 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-3 R<sub>6</sub>, Y, -(C=O)Y, -(CH<sub>2</sub>)Y, and -(CH(CN))Y;

R<sub>9</sub> is selected from the group consisting of halogen, cyano, -N(SO<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>, -SO<sub>2</sub>NH<sub>2</sub>, halo(C<sub>1-2</sub>)alkyl, C<sub>1-3</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl);

R<sub>5B</sub> represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, amino, C<sub>1-4</sub>alkyl, and C<sub>1-2</sub>alkoxy; and

R<sub>9B</sub> represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, and C<sub>1-2</sub>alkyl, and C<sub>1-2</sub>alkoxy.

64. A compound or salt according to Claim 63, wherein:

R<sub>6</sub> is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -NH(C<sub>1-4</sub>alkyl), and -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl) and Y; and

Y is independently selected at each occurrence from C<sub>3-8</sub> cycloalkyl, piperidinyl, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl, each of which may be further substituted with

one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, mono- or di(C<sub>1-4</sub>)alkylamino, and C<sub>1-4</sub>alkylthio.

65. A compound or salt according to Claim 63, wherein: R<sub>9</sub> is cyano, trifluoromethyl, chloro, or iodo; and R<sub>9B</sub> is hydrogen.

66. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

67. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-cyclohexylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

68. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

69. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

70. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-isopropylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

71. A compound according to Claim 50, which is (2S)-4-(3-chloropyridin-2-yl)-N-(4-trifluoromethylphenyl)-2-

methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

72. A compound according to Claim 50, which is (2S)-N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

73. A compound according to Claim 50, which is (2S)-4-(3-chloropyridin-2-yl)-N-(4-isopropylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

74. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-(4-piperidin-1-ylphenyl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

75. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[2-fluoro-4-(trifluoromethyl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

76. A compound according to Claim 50, which is (2R)-2-methyl-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

77. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

78. A compound according to Claim 50, which is (2R)-N-(4-isopropylphenyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-



yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

79. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-2,6-dimethyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

80. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2,6-dimethylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

81. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-N-(4-isopropylphenyl)-2,6-dimethylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

82. A compound according to Claim 50, which is (2R)-N-(4-cyclohexylphenyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

83. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-N-(4-cyclohexylphenyl)-2,6-dimethylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

84. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-cyclopentylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

85. A compound according to Claim 50, which is (2R)-N-(4-cyclopentylphenyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

86. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-[3-(dimethylamino)pyridin-2-yl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

87. A compound according to Claim 50, which is (2R)-4-[3-(dimethylamino)pyridin-2-yl]-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

88. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-(3-methoxypyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

89. A compound according to Claim 50, which is (2R)-4-(3-methoxypyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

90. A compound according to Claim 50, which is (2R)-N-(4-cyclohexylphenyl)-4-(3-methoxypyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

91. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(3,6-dihydro-2H-pyran-4-yl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

92. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-(4-tetrahydro-2H-pyran-4-ylphenyl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

93. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(4-hydroxytetrahydro-2H-pyran-4-yl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

94. A compound according to Claim 50, which is (2R)-N-[4-(4-hydroxytetrahydro-2H-pyran-4-yl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

95. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[4-(2-methyl-1,3-thiazol-4-yl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

96. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(2-ethyl-1,3-thiazol-4-yl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

97. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(2-methoxy-1,1-dimethylethyl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

98. A compound according to Claim 50, which is (2R)-N-[4-(2-methoxy-1,1-dimethylethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

99. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(1-cyano-1-methylethyl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

100. A compound according to Claim 50, which is (2R)-N-[4-(1-cyano-1-methylethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

101. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2-ethylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

102. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-2-ethyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

103. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-2-ethyl-N-(4-isopropylphenyl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

104. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-2-ethyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

105. A compound according to Claim 50, which is 2-ethyl-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

106. A compound according to Claim 50, which is 2-ethyl-N-(4-isopropylphenyl)-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

107. A compound according to Claim 50, which is 2-tert-butyl-N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

108. A compound according to Claim 50, which is 2-tert-butyl-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

109. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2-isopropylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

110. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-2-isopropyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

111. A compound according to Claim 50, which is 2-isopropyl-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)

pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

112. A compound according to Claim 50, which is 2-isopropyl-N-(4-isopropylphenyl)-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

113. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

114. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-(3-fluoropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

115. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-N-(4-isopropylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

116. A compound according to Claim 50, which is (2R)-N-(4-cyclohexylphenyl)-4-(3-fluoropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

117. A compound according to Claim 50, which is (2R)-N-(4-cyclopentylphenyl)-4-(3-fluoropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

118. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-(3-cyanopyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

119. A compound according to Claim 50, which is (2R)-4-(3-cyanopyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

120. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-{4-[cyano(phenyl)methyl] phenyl}-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

121. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[3-methyl-4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

122. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-[3-methyl-4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

123. A compound according to Claim 50, which is (2R)-4-{3-[bis(methylsulfonyl)amino]pyridin-2-yl}-N-(4-tert-butylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

124. A compound according to Claim 50, which is (2R)-2-methyl-N-[3-methyl-4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl] piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

125. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-{4-[1-(trifluoromethyl)vinyl]phenyl} piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

126. A compound according to Claim 50, which is (2R)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]-N-{4-[1-(trifluoromethyl)vinyl] phenyl}piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

127. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-{4-[1-(trifluoromethyl)vinyl] phenyl}piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

128. A compound according to Claim 50, which is (2R)-N-(4-sec-butylphenyl)-4-(3-fluoropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

129. A compound according to Claim 50, which is (2R)-2-methyl-N-[4-(2,2,2-trifluoro-1-methylethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

130. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-[4-(2,2,2-trifluoro-1-methylethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

131. A compound according to Claim 50, which is (2R)-4-(3-chloro-5-nitropyridin-2-yl)-2-methyl-N-[4-



(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

132. A compound according to Claim 50, which is (2R)-4-(5-amino-3-chloropyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

133. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-N-[3-fluoro-4-(trifluoromethyl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

134. A compound according to Claim 50, which is (2R)-N-[3-fluoro-4-(trifluoromethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

135. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[4-(2,2,2-trifluoro-1-methylethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

136. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

137. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

138. A compound according to Claim 50, which is (2R)-2-methyl-N-(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

139. A compound according to Claim 50, which is (2R)-4-[3-(aminosulfonyl)pyridin-2-yl]-N-(4-tert-butylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

140. A compound according to Claim 50, which is (2R)-N-(4-benzoylphenyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

141. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-iodophenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

142. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-{4-[2,2,2-trifluoro-1,1-bis(trifluoromethyl)ethyl]phenyl}piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

143. A compound according to Claim 50, which is (2R)-2-methyl-N-{4-[2,2,2-trifluoro-1,1-bis(trifluoromethyl)ethyl]phenyl}-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

144. A compound according to Claim 50, which is (2R)-N-(4-butylphenyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

145. A compound according to Claim 50, which is 2-(fluoromethyl)-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

146. A compound according to Claim 50, which is (2R)-N-[4-bromo-3-(trifluoromethyl)phenyl]-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

147. A compound according to Claim 50, which is (2R)-N-[4-bromo-3-(trifluoromethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

148. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

149. A compound according to Claim 50, which is (2R)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

150. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-{4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]phenyl}piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

151. A compound according to Claim 50, which is (2R)-2-methyl-N-{4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)

ethyl]phenyl}-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

152. A compound according to Claim 40, which is (2R)-N-(4-tert-butylphenyl)-4-(3-chloropyrazin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

153. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-N-(4-isopropylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

154. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

155. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-2-methyl-N-{4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl] phenyl} piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

156. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-2-methyl-N-{4-cyclopentyl-phenyl} piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

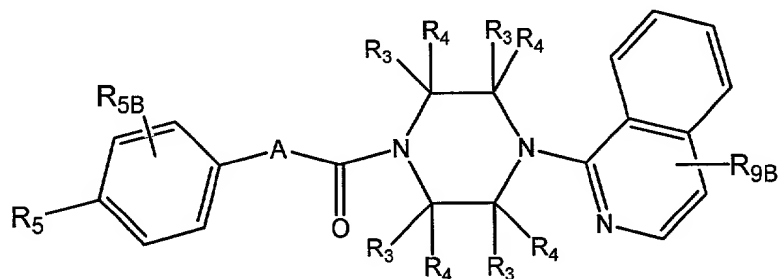
157. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-2-methyl-N-{4-cyclohexyl-phenyl} piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

158. A compound according to Claim 42, which is 4-(3-chloropyridin-2-yl)-N-[5-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

159. A compound according to Claim 42, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[5-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

160. A compound according to Claim 42, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[6-(trifluoromethyl)pyridin-3-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

161. A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S,  $\text{NR}_A$ ,  $\text{CR}_B\text{R}_B'$ ,  $\text{NR}_A\text{CR}_B\text{R}_B'$ ,  $\text{CR}_B\text{R}_B'\text{NR}_A$ ,  $-\text{CR}_A=\text{CR}_B-$ , and  $\text{C}_3\text{H}_4$ ; where  $\text{R}_A$ ,  $\text{R}_B$ , and  $\text{R}_B'$  are independently selected at each occurrence from hydrogen or  $\text{C}_{1-6}$  alkyl;

$\text{R}_3$  and  $\text{R}_4$  are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo( $\text{C}_{1-6}$ )alkyl, halo( $\text{C}_{1-6}$ )alkoxy, hydroxy, amino,  $\text{C}_{1-6}$ alkyl,

C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), and -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl);

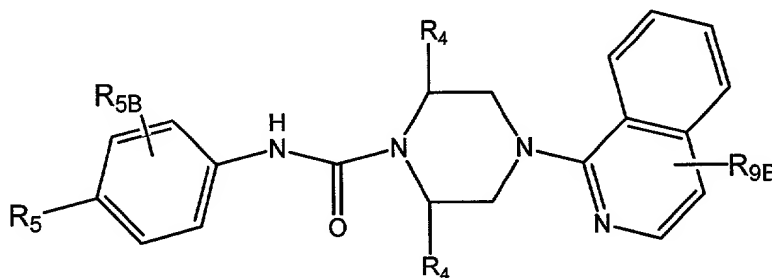
R<sub>5</sub> is selected from the group consisting of halogen, halo(C<sub>1-6</sub>)alkyl, C<sub>3-6</sub>alkyl substituted with 0-3 R<sub>6</sub>, C<sub>2-6</sub>alkenyl substituted with 0-3 R<sub>6</sub>, (C<sub>3-8</sub>cycloalkyl)C<sub>1-4</sub>alkyl substituted with 0-3 R<sub>6</sub>, and Y;

R<sub>5B</sub> and R<sub>9B</sub> each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, amino, C<sub>1-4</sub>alkyl, and C<sub>1-2</sub>alkoxy;

R<sub>6</sub> is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, -NH(C<sub>1-4</sub>alkyl), and -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl) and Y;

Y is independently selected at each occurrence from C<sub>3-8</sub> cycloalkyl, piperidiny, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl, each of which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, mono- or di(C<sub>1-4</sub>)alkylamino, and C<sub>1-4</sub>alkylthio.

162. A compound or salt according to Claim 161 of the Formula:



wherein

R<sub>4</sub> is independently selected at each occurrence from hydrogen and C<sub>1-4</sub>alkyl.

163. A compound or salt according to Claim 162, wherein: R<sub>5</sub> is selected from the group consisting of halo(C<sub>1-6</sub>)alkyl, C<sub>3-6</sub>alkyl, (C<sub>3-8</sub>cycloalkyl)C<sub>1-4</sub>alkyl, and Y;

R<sub>5B</sub> and R<sub>9B</sub> each represent from 0 to 1 substituents and are independently chosen from halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, amino, C<sub>1-4</sub>alkyl, and C<sub>1-2</sub>alkoxy;

Y is selected from C<sub>3-8</sub> cycloalkyl, piperidinyl, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl.

164. A compound according to Claim 161, which is (2R)-4-isoquinolin-1-yl-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

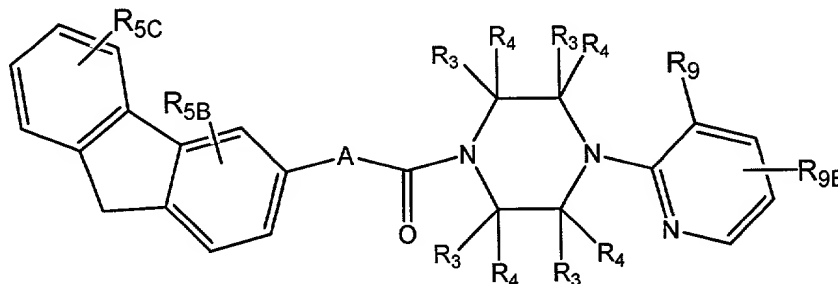
165. A compound according to Claim 161, which is (2R)-N-(4-tert-butylphenyl)-4-isoquinolin-1-yl-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

166. A compound according to Claim 161, which is (2R)-N-(4-isopropylphenyl)-4-isoquinolin-1-yl-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

167. A compound according to Claim 161, which is (2R)-N-(4-cyclopentylphenyl)-4-isoquinolin-1-yl-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

168. A compound according to Claim 161, which is (2R)-N-(4-cyclohexylphenyl)-4-isoquinolin-1-yl-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

169. A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S,  $\text{NR}_A$ ,  $\text{CR}_B\text{R}_B'$ ,  $\text{NR}_A\text{CR}_B\text{R}_B'$ ,  $\text{CR}_B\text{R}_B'\text{NR}_A$ ,  $-\text{CR}_A=\text{CR}_B-$ , and  $\text{C}_3\text{H}_4$ ; where  $\text{R}_A$ ,  $\text{R}_B$ , and  $\text{R}_B'$  are independently selected at each occurrence from hydrogen or  $\text{C}_{1-6}$  alkyl;

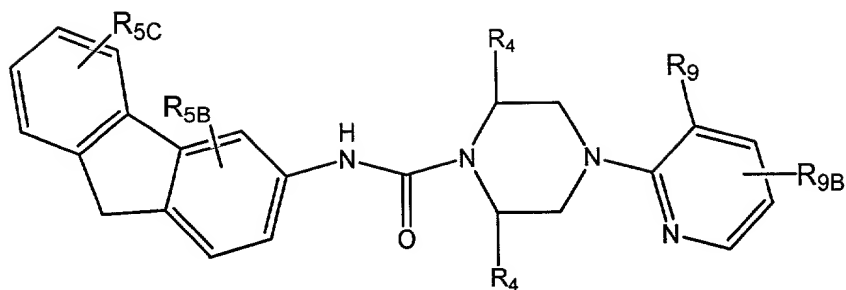
$\text{R}_3$  and  $\text{R}_4$  are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo( $\text{C}_{1-6}$ )alkyl, halo( $\text{C}_{1-6}$ )alkoxy, hydroxy, amino,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{2-6}$ alkenyl,  $\text{C}_{2-6}$ alkynyl,  $\text{C}_{1-6}$ alkoxy,  $-\text{NH}(\text{C}_{1-6}\text{alkyl})$ , and  $-\text{N}(\text{C}_{1-6}\text{alkyl})(\text{C}_{1-6}\text{alkyl})$ ;

$\text{R}_{5B}$ ,  $\text{R}_{5C}$ , and  $\text{R}_{9B}$  each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo( $\text{C}_{1-2}$ )alkyl, halo( $\text{C}_{1-2}$ )alkoxy, amino,  $\text{C}_{1-4}$ alkyl, and  $\text{C}_{1-2}$ alkoxy; and

$\text{R}_9$  is selected from the group consisting of halogen, cyano,  $-\text{N}(\text{SO}_2\text{CH}_3)_2$ ,  $-\text{SO}_2\text{NH}_2$ , halo( $\text{C}_{1-3}$ )alkyl,  $\text{C}_{1-3}$ alkoxy,  $-\text{NH}(\text{C}_{1-3}\text{alkyl})$ , and  $-\text{N}(\text{C}_{1-3}\text{alkyl})(\text{C}_{1-3}\text{alkyl})$

170. A compound or salt according to Claim 169 of the Formula:





wherein

R<sub>4</sub> is independently selected at each occurrence from hydrogen and C<sub>1-4</sub>alkyl.

171. A compound or salt according to Claim 170, wherein: R<sub>9</sub> is selected from the group consisting of halogen and halo(C<sub>1-2</sub>)alkyl; and R<sub>5B</sub> and R<sub>9B</sub> each represent from 0 to 1 substituents and are independently chosen from halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, amino, C<sub>1-4</sub>alkyl, and C<sub>1-2</sub>alkoxy.

172. A compound according to Claim 169, which is (2R)-4-(3-chloropyridin-2-yl)-N-(9H-fluoren-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

173. A compound according to Claim 169, which is (2R)-N-(9H-fluoren-2-yl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

174. A compound according to Claim 38, which is (2R)-N-(4-tert-butylcyclohexyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

175. A compound according to Claim 38, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-isopropylcyclohexyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

176. A compound according to Claim 38, which is (2R)-N-(4-isopropylcyclohexyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

177. A method of reducing the calcium conductance of a capsaicin receptor, which method comprises: contacting a first solution comprising a fixed concentration of a capsaicin receptor agonist and a compound or salt of Claim 50 with a cell expressing the capsaicin receptor, wherein the compound or salt is present in the solution at a concentration sufficient to produce a detectable reduction of the calcium mobilization effects of the capsaicin receptor agonist when tested in an *in vitro* assay in which cells expressing a capsaicin receptor are contacted with a second solution comprising the fixed concentration of capsaicin receptor agonist and the compound or salt.

178. The method of Claim 177 wherein the cell expressing the capsaicin receptor is a neuronal cell that is contacted *in vivo* in an animal, and wherein the first solution is a body fluid of said animal.

179. The method of Claim 177 wherein the animal is a human patient.

180. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or salt of Claim 50.

181. A package comprising a pharmaceutical composition of claim 180 in a container and further comprising indicia comprising instructions for using the composition to alleviate pain.

182. A package comprising a pharmaceutical composition of claim 180 in a container and further comprising indicia comprising instructions for using the composition to treat a patient suffering from urinary incontinence.

183. A package comprising a pharmaceutical composition of claim 180 in a container and further comprising indicia comprising instructions for using the composition to alleviate symptoms of exposure to capsaicin or tear gas.

184. A compound or salt of Claim 50 wherein, in an in vitro assay of capsaicin receptor antagonism, the compound or salt exhibits capsaicin receptor antagonist activity, but in an in vitro assay of capsaicin receptor agonism the compound does not exhibit detectable agonist activity.

185. A compound or salt of Claim 50 wherein a dose of the compound or salt that is twice the minimum dose sufficient to provide analgesia in an animal model for determining pain relief does not produce sedation in an animal model assay of sedation.

186. A method of treating a mammal suffering from at least one symptom selected from the group consisting of symptoms of

exposure to capsaicin, symptoms of burns or irritation due to exposure to heat, symptoms of burns or irritation due to exposure to light, symptoms of burns, bronchoconstriction or irritation due to exposure to tear gas, and symptoms of burns or irritation due to exposure to acid, the method comprising administering to the mammal a therapeutic dose of a compound that is a high potency capsaicin receptor antagonist in an *in vitro* assay of capsaicin receptor antagonism, is not a capsaicin analog; wherein the therapeutic dose contains an amount of the compound that is effective to reduce severity of at least one of said at least one symptom.

187. The method of claim 186 wherein the compound is a compound or salt of any of claims 1-176.

188. A method of treating a mammal suffering from neuropathic pain, the method comprising administering to the mammal a therapeutically effective amount of a compound that is a high potency capsaicin receptor antagonist in an *in vitro* assay of capsaicin receptor antagonism.

189. A method of treating a mammal suffering from peripheral-nerve-mediated pain, the method comprising administering to the mammal a therapeutic dose of a compound that is a capsaicin receptor antagonist, wherein the compound is a high potency capsaicin receptor antagonist in an *in vitro* assay of capsaicin receptor antagonism and is not a capsaicin analog,

wherein the therapeutic dose contains an amount of the compound that is effective to reduce the peripheral-nerve-mediated pain.

190. The method of Claim 189 wherein the compound is a compound or salt of Claim 50.

191. The method of claim 189 wherein the pain is neuropathic pain.

192. The method of Claim 190 wherein the pain is associated with a condition selected from the group consisting of postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, Charcot's pain, toothache, venomous snake bite, spider bite, insect sting, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, sciatic neuritis, peripheral neuritis, polyneuritis, optic neuritis, postfebrile neuritis, migrating neuritis, segmental neuritis, Gombault's neuritis, neuronitis, cervicobrachial neuralgia, cranial neuralgia, geniculate neuralgia, glossopharyngeal neuralgia, migranous neuralgia, idiopathic neuralgia, intercostals neuralgia, mammary neuralgia, mandibular joint neuralgia, Morton's neuralgia, nasociliary neuralgia, occipital neuralgia, red neuralgia, Sluder's neuralgia, splenopalatine neuralgia, supraorbital neuralgia, vidian neuralgia, sinus headache, tension headache, labor, childbirth, intestinal gas, menstruation, cancer, and trauma.

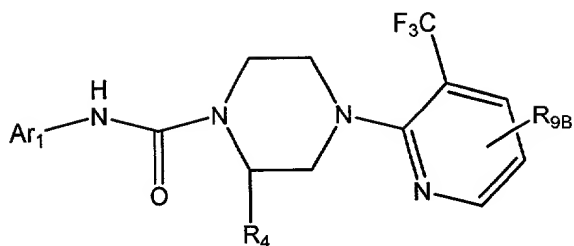
193. A compound or salt of Claim 50 wherein the compound or salt is not addictive.

194. The use of a compound according to Claim 1, 4, 9, 31, or 50 for the manufacture of a medicament for the treatment of pain.

195. The use of a compound according to Claim 1, 4, 9, 31, or 50 for the manufacture of a medicament for the treatment of neuropathic pain.

196. The use of a compound according to Claim 1, 4, 9, 31, or 50 for the manufacture of a medicament for the treatment of the pain associated with a condition selected from the group consisting of postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, Charcot's pain, toothache, venomous snake bite, spider bite, insect sting, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, sciatic neuritis, peripheral neuritis, polyneuritis, optic neuritis, postfebrile neuritis, migrating neuritis, segmental neuritis, Gombault's neuritis, neuronitis, cervicobrachial neuralgia, cranial neuralgia, geniculate neuralgia, glossopharyngeal neuralgia, migranous neuralgia, idiopathic neuralgia, intercostals neuralgia, mammary neuralgia, mandibular joint neuralgia, Morton's neuralgia, nasociliary neuralgia, occipital neuralgia, red neuralgia, Sluder's neuralgia, splenopalatine neuralgia, supraorbital neuralgia, vidian neuralgia, sinus headache, tension headache, labor, childbirth, intestinal gas, menstruation, cancer, and trauma.

197. A compound of the Formula



or a pharmaceutically acceptable salt thereof wherein:

R<sub>4</sub> is methyl or hydrogen;

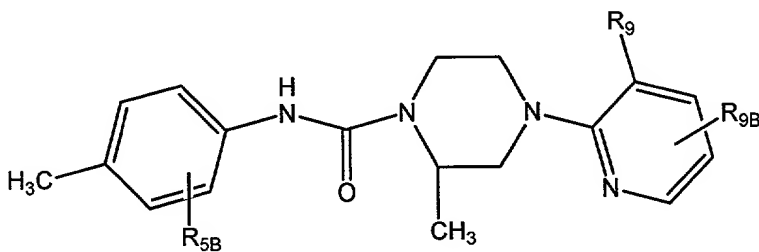
R<sub>9B</sub> represents 0-2 substituents independently chosen from:

halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy,

amino, C<sub>1-4</sub>alkyl, and C<sub>1-2</sub>alkoxy; and

Ar<sub>1</sub> is 2,4-dichlorophenyl or 3-nitro-4-chlorophenyl.

198. A compound of the Formula



or a pharmaceutically acceptable salt thereof wherein:

R<sub>9</sub> is chloro or trifluoromethyl; and

R<sub>5B</sub> and R<sub>9B</sub> independently represent from 0-2 substituents on each

of the rings on which they occur and are independently chosen from: halogen, cyano, nitro, halo(C<sub>1-2</sub>)alkyl, halo(C<sub>1-2</sub>)alkoxy, amino, C<sub>1-4</sub>alkyl, and C<sub>1-2</sub>alkoxy.